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Sequencing the Human Genome

A molecular biologist might say, "The proper study of mankind is the bacterium." The developmental biologist would say, "The proper study of mankind is the fruit fly." The cancer expert says, "The proper study of mankind is the rat." The poet said, "The proper study of mankind is man." All are, of course, partly right and partly wrong. The universality of the genetic code and of metabolic systems means that very different forms of life reveal principles and facts that are relevant to human health and illness. Although each species is interesting in itself, the major reason that research in other species is so strongly supported by Congress is its applicability to human beings. Therefore, the obvious answer as to whether the human genome should be sequenced is, "Yes. Why do you ask?"

The more pertinent question about sequencing is how fast and how much. Major portions of the human genome will be uncovered in bits and pieces with laboratories operating in conventional ways. Yet this sequencing is being done inefficiently because each laboratory must learn the methods, develop its own cloning libraries, and operate with techniques and equipment that could be vastly improved. A massive assault—developing new techniques, creating systematic libraries, coordinating data—would inevitably produce the answer sooner. Large segments of repetitive and "junk" DNA, which may have little use according to current concepts, would be sequenced, but even so the gains in new techniques would more than compensate for the delays of uninteresting stretches.

The next question is who should do the job. The National Institutes of Health has funded most of the scientists who have made the project possible, but it would be in danger of a Big Science–Little Science conflict. The Department of Energy has only a few scientists in the proper leadership area, but has had experience with large projects and offers a political arrangement that could ensure that the program is an add-on, not a subtraction from Little Science.

For this project to command the respect and support of the biological community, acknowledged experts are needed on the governing board of the project. (A National Academy of Sciences committee now studying the whole problem is a blue-ribbon list for selection of such a board.) The program and individual grant requests should be peer reviewed continuously, following the excellent procedures of NIH and the National Science Foundation. Leaders from NIH, NSF, the Howard Hughes Medical Institute, and foreign scientists should play prominent roles in the organization. A DOE program should be expected to use national laboratory personnel for some of the work but to act more as a nerve center, both monitoring and administering a large number of smaller grants to investigators located all over the world. This effort should be international with contributions from different countries in terms of grants, investigators, and leadership advice. A plan in which DOE recognizes the importance of peer review and decentralized administration would thus be a compromise, but it would ensure proper quality and avoid a budget situation that placed Big Science and Little Science in dangerously direct financial competition. An alternative would be to try to set up within NIH a special institute for sequencing. Political memories are short, however, and soon that allocation would be thought of as "NIH funds," creating the unwanted competition between "big" applied and "little" investigator-initiated research. It would appear that DOE could find the leadership excellence more easily than NIH could provide the budgetary insulation.

The implications of sequencing the human genome are staggering. The recent discoveries of genes identified with muscular dystrophy, manic depression, cystic fibrosis, and Alzheimer's disease are illustrative aspects of the potential. Human subjects have been a source of information, medically, psychologically, and evolutionarily for centuries. They offer a wealth of information in regard to basic biology that is not duplicated by any other species. Hereditary defects may be able to be diagnosed more efficiently and eventually eliminated. Moreover, developing the successful methodology for sequencing the human genome means that understanding other species will also be accelerated. The opportunities are enormous. We have been "walking along the chromosomes" long enough. It is time to start running.—DANIEL E. KOSHLAND, JR.